

AMENDMENTS TO THE CLAIMS:

Please amend the claims as shown below. A complete listing of the claims, including their current status identifiers, is set forth below.

1. (Currently Amended) A method for detecting a GPCR-binding partner complex comprising a GPCR and a GPCR binding partner, said method comprising:

(a) culturing a cell producing a first and a second polypeptide, wherein at least one of said first and said second polypeptides is a GPCR,

(b) lysing said cell, **thereby producing a cell lysate;**

(c) **capturing said first polypeptide of said cell lysate, wherein said capturing comprises** contacting said first polypeptide with a substrate having affinity for said first polypeptide, under conditions suitable for binding of said first polypeptide to said substrate; and

(d) detecting the presence of said second polypeptide on said substrate, wherein said detecting is direct;

wherein said method does not comprise immunoprecipitating said first and second polypeptides and wherein the presence of said second polypeptide on said substrate is indicative of a GPCR-binding partner complex.

2. (Previously Presented) The method of claim 1, wherein said first polypeptide is a GPCR and said second polypeptide is a GPCR binding partner.

3. (Original) The method of claim 1, wherein said first polypeptide is a GPCR binding partner and said second polypeptide is a GPCR.

4. (Original) The method of claim 1, wherein at least one of said first and said second polypeptides is an orphan GPCR.

5. (Original) The method of claim 1, wherein at least one of said first and second polypeptides is a native GPCR.

6. (Canceled)

7. (Original) The method of claim 1, wherein both of said first and said second polypeptides are GPCRs.

8-11 (Canceled)

12. (Original) The method of claim 1, wherein at least one of said first and said second polypeptides is recombinant.

13-22 (Canceled)

23. (Original) The method of claim 1, wherein said first and said second polypeptides are endogenously co-expressed in at least one cell type, tissue, or tissue sub-region.

24. (Previously Presented) The method of claim 1, wherein said method further comprises selecting prior to said culturing step (a) said first and said second polypeptides wherein said first and said second polypeptides are coexpressed in a least one cell type, tissue or tissue sub-region.

25. (Currently Amended) A method for detecting a GPCR-binding partner complex comprising a GPCR and a GPCR binding partner, said method comprising:

(a) culturing a cell producing a first and a second polypeptide, wherein at least one of said first and said second polypeptides is a GPCR,

(b) lysing said cell, **thereby producing a cell lysate;**

(c) **capturing said first polypeptide of said cell lysate, wherein said capturing comprises** contacting said first polypeptide with an addressable substrate having affinity for said

first polypeptide, under conditions suitable for binding of said first polypeptide to said substrate in an addressable manner; and

(d) detecting the presence of said second polypeptide on said substrate, wherein said detecting is direct;

wherein said method does not comprise immunoprecipitating said first and second polypeptides and wherein the presence of said second polypeptide on said substrate is indicative of a GPCR-binding partner complex.

26. (Original) The method of claim 25, wherein said first polypeptide is a GPCR and said second polypeptide is a GPCR binding partner.

27. (Original) The method of claim 25, wherein said first polypeptide is a GPCR binding partner and said second polypeptide is a GPCR.

28. (Original) The method of claim 25, wherein at least one of said first and said second polypeptides is an orphan GPCR.

29. (Original) The method of claim 25, wherein at least one of said first and said second polypeptides is a native GPCR.

30. (Canceled)

31. (Original) The method of claim 25, wherein both of said first and said second polypeptides are GPCRs.

32-35 (Canceled)

36. (Original) The method of claim 25, wherein at least one of said first and said second polypeptides is recombinant.

37-51 (Canceled)

52. (Previously Presented) The method of claim 25, wherein said first and said second polypeptides are endogenously co-expressed in at least one cell type, tissue, or tissue sub-region.

53. (Previously Presented) The method of claim 25, wherein said method further comprises selecting prior to said culturing step (a) said first and said second polypeptides wherein said first and said second polypeptides are coexpressed in a least one cell type, tissue or tissue sub-region.

54. (Previously Presented) A method of identifying whether a candidate polypeptide is a binding partner for a GPCR, comprising the step of detecting a GPCR-binding partner complex comprising said candidate polypeptide and said GPCR according to the method of claim 1 or claim 25, wherein detection of said complex is indicative of said candidate polypeptide being a binding partner of said GPCR.

55. (Currently Amended) A method for detecting a GPCR-binding partner complex, said method comprising:

(a) culturing a plurality of cells, each cell producing a first and a second polypeptide, wherein said second polypeptide is fused to a reporter protein, wherein at least one of said first and said second polypeptides is a GPCR, and wherein each cell produces a different GPCR;

(b) lysing said cells, **thereby producing a plurality of cell lysates;**

(c) **capturing said first polypeptides of said plurality of cell lysates, wherein said capturing comprises** contacting said first polypeptide from each cell with an addressable substrate having affinity for said first polypeptide, under conditions suitable for binding of said first polypeptide to said substrate at an address specific for said cell; and

(d) detecting the presence of said second polypeptide on said substrate, wherein said detecting is direct;

wherein said method does not comprise immunoprecipitating said first and second polypeptides and wherein the presence of said second polypeptide at an address on said

substrate is indicative of a GPCR-binding partner complex comprising said first polypeptide and said second polypeptides produced by the cell having said address.

56. (Original) The method of claim 55 wherein said plurality of cells is at least 2, at least 5, at least 10, at least 15, at least 20, at least 25, at least 50, or at least 100 cells.

57. (Original) The method of claim 55, wherein said first and said second polypeptides are endogenously co-expressed in at least one cell type, tissue, or tissue sub-region.

58. (Original) The method of claim 55, wherein said method further comprises selecting prior to said culturing step (a) said first and said second polypeptides wherein said first and said second polypeptides are coexpressed in a least one cell type, tissue or tissue sub-region.

59. (Currently Amended) A method for detecting-a GPCR-binding partner complex, said method comprising:

(a) culturing a cell, said cell producing a first and a plurality of a second polypeptide, wherein each of said second polypeptides is fused to a reporter protein, wherein each of said plurality of said second polypeptide is different and wherein at least one of said first and said plurality of said second polypeptide is a GPCR;

(b) lysing said cell, **thereby producing a cell lysate;**

(c) **capturing said first polypeptide, wherein said capturing comprises** contacting said first polypeptide with a substrate having affinity for said first polypeptide, under conditions suitable for binding of said first polypeptide to said substrate; and

(d) detecting the presence of said second polypeptide on said substrate, wherein said detecting is done directly using said reporter protein;

wherein said method does not comprise immunoprecipitating said first and second polypeptides and wherein the presence of said second polypeptide on said substrate is indicative of at least one GPCR-binding partner complex comprising said first polypeptide and said second polypeptide.

60. (Original) The method of claim 59 wherein said GPCR-binding partner complex is detected, further comprising repeating steps (a) to (d) one or more times with subsets of said plurality of said second polypeptide, said subsets encompassing said plurality, until a GPCR-binding partner complex is detected from at least one cell producing a said first polypeptide and a single said second polypeptide.

61. (Original) The method of claim 59 wherein said plurality of said second polypeptides is at least 2, at least 5, at least 10, at least 15, at least 20, at least 25 said, at least 50, or at least 100 of second polypeptide.

62. (Canceled)

63. (Original) The method of claim 59, wherein said first and second polypeptides are endogenously co-expressed in at least one cell type, tissue, or tissue sub-region.

64. (Original) The method of claim 59, wherein said method further comprises selecting prior to said culturing step (a) said first and said second polypeptides wherein said first and said second polypeptides are coexpressed in a least one cell type, tissue or tissue sub-region.

65. (Previously Presented) The method of any one of claim 55 or claim 59, wherein said first polypeptide is a GPCR and said second polypeptide is a GPCR binding partner.

66. (Previously Presented) The method of claim 55 or claim 59, wherein said first polypeptide is a GPCR binding partner and said second polypeptide is a GPCR.

67. (Previously Presented) The method of claim 55 or claim 59, wherein at least one of said first and said second polypeptides is an orphan GPCR.

68. (Previously Presented) The method of claim 55 or claim 59, wherein at least one of said first and said second polypeptide is a native GPCR.

69. (Canceled)

70. (Previously Presented) The method of claim 55 or claim 59, wherein both of said first and said second polypeptides are GPCRs.

71-74 (Canceled)

75. (Previously Presented) The method of claim 55 or claim 59, wherein at least one of said first and second polypeptides is recombinant.

76-90 (Canceled)

91. (Previously Presented) The method according to any one of claims 1, 25, 55 and 59 wherein said first and said second polypeptides are both mammalian.

92. (Previously Presented) The method according to any one of claims 1, 25, 55 and 59 wherein said first and second polypeptides are both human.

93-121 (Canceled)

122. (New) The method of claim 1, wherein said first polypeptide comprises an affinity tag, and said contacting step comprises binding said affinity tag to the affinity substrate.

123. (New) The method of claim 122, wherein said affinity tag is an epitope tag.

124. (New) The method of claim 123, wherein said binding comprises using an antibody specific for said epitope tag.

125. (New) The method of claim 123, wherein said epitope tag is an HA tag.

126. (New) The method of claim 1, wherein said second polypeptide is detectably labeled, and said detecting step comprises detecting said detectable label.

127. (New) The method of claim 1, wherein said second polypeptide is fused to a reporter protein.

128. (New) The method of claim 127, wherein said reporter protein is luciferase.

129. (New) The method of claim 1, wherein said cell lysate is a whole cell lysate.

130. (New) The method of claim 1, wherein said cell lysate is a lysate of isolated membrane.

131. (New) The method of claim 25, wherein said first polypeptide comprises an affinity tag, and said contacting step comprises binding said affinity tag to the affinity substrate.

132. (New) The method of claim 131, wherein said affinity tag is an epitope tag.

133. (New) The method of claim 132, wherein said binding comprises using an antibody specific for said epitope tag.

134. (New) The method of claim 132, wherein said epitope tag is an HA tag.

135. (New) The method of claim 25, wherein said second polypeptide is detectably labeled, and said detecting step comprises detecting said detectable label.

136. (New) The method of claim 25, wherein said second polypeptide is fused to a reporter protein.

137. (New) The method of claim 136, wherein said reporter protein is luciferase.

138. (New) The method of claim 25, wherein said cell lysate is a whole cell lysate.

139. (New) The method of claim 25, wherein said cell lysate is a lysate of isolated membrane.

140. (New) The method of claim 55, wherein said first polypeptide comprises an affinity tag, and said contacting step comprises binding said affinity tag to the affinity substrate.

141. (New) The method of claim 140, wherein said affinity tag is an epitope tag.

142. (New) The method of claim 141, wherein said binding comprises using an antibody specific for said epitope tag.

143. (New) The method of claim 141, wherein said epitope tag is an HA tag.

144. (New) The method of claim 55, wherein said second polypeptide is detectably labeled, and said detecting step comprises detecting said detectable label.

145. (New) The method of claim 55, wherein said second polypeptide is fused to a reporter protein.

146. (New) The method of claim 145, wherein said reporter protein is luciferase.

147. (New) The method of claim 55, wherein said cell lysate is a whole cell lysate.

148. (New) The method of claim 55, wherein said cell lysate is a lysate of isolated membrane.

149. (New) The method of claim 59, wherein said first polypeptide comprises an affinity tag, and said contacting step comprises binding said affinity tag to the affinity substrate.

150. (New) The method of claim 149, wherein said affinity tag is an epitope tag.

151. (New) The method of claim 150, wherein said binding is done using an antibody specific for said epitope tag.

152. (New) The method of claim 150, wherein said epitope tag is an HA tag.

153. (New) The method of claim 59, wherein said second polypeptide is detectably labeled, and said detecting step comprises detecting said detectable label.

154. (New) The method of claim 59, wherein said second polypeptide is fused to a reporter protein.

155. (New) The method of claim 154, wherein said reporter protein is luciferase.

156. (New) The method of claim 59, wherein said cell lysate is a whole cell lysate.

157. (New) The method of claim 59, wherein said cell lysate is a lysate of isolated membrane.